EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Human Use (CHMP)

Scientific conclusions and grounds for the variation to the terms of the marketing authorisation(s)

Active substance(s): pramipexole

Procedure No. EMEA/H/C/PSUSA/00002491/201604

Period covered by the PSUR: 7 April 2013 – 6 April 2016

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Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for pramipexole, the scientific conclusions of CHMP are as follows:

Dopamine agonist withdrawal syndrome (DAWS)

In the reporting period four published papers described five cases of DAWS following withdrawal of pramipexole. In two cases, the event improved or resolved after reintroduction of pramipexole, thus demonstrating positive dechallenge.

Cumulative evidences include three recently published observational studies, one of them with a prospective design. In a study from 2010, DAWS occurred in five of 26 subjects undergoing DA taper. All five subjects were tapered off pramipexol. For two patients, positive re- and dechallenge was described, in one of them multiple times. In two other studies, of 84 and 51 patients withdrawn from DA therapy, 13 and 12 developed DAWS, five and four of them using pramipexole, respectively. This corresponds to a DAWS frequency of 15, 19 and 24% of patients discontinuing DAs in the three studies.

The proposed mechanism for the syndrome is related to that of impulse control disorder and other addiction disorders associated with a reward deficiency state due to a dysfunction of the mesocorticolimbic dopaminergic pathways.

Based on the available data the PRAC concluded that a warning to add further information on “dopamine agonist withdrawal syndrome” (DAWS) with reference to section 4.2 and 4.8 where DAWS should also be added as an adverse reaction with a frequency of not known should be included in the product information.

Therefore, in view of the data presented in the reviewed PSURs, the PRAC considered that changes to the product information of medicinal products containing pramipexole were warranted.

In the RMP, the risk “abnormal behaviour” should be amended to “impulse control behaviour”, and the risk “response-based behaviour” should be changed to “dopamine dysregulation syndrome”.

The CHMP agrees with the scientific conclusions made by the PRAC.

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for pramipexole the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing pramipexole is unchanged subject to the proposed changes to the product information

The CHMP recommends that the terms of the marketing authorisation(s) should be varied.